Fig. 1

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841 nildvqtttg echfenyqrv caleqqksam qtlkgivrfl sktdkrllyc ikadphclnf
901 lcnfgkmesg keasvhiqle grpsilemde tsalkfeira tgfpepnprv ielnkdenva
961 hvlleglhhq rpkryftivi isssllgli vlllisyvmw kagffkrqyk silqeenrrd
1021 swsyinsksn dd

Fig. 2

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121 lrlrsgepqt ftlkfkraed ypidlyylmd lsysmkddle nvkslgtdlm nemrritsdf
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Fig. 3A

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Fig. 3B

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301 rkevelivqa fprdpeiems gglvngssvt vsckvpsvyp ldrleiellk getilenief
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421 dttvlvspss ileegssvnm tclsqgfpap kilwsrqlpn gelqplsena tltlistkme
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Fig. 4

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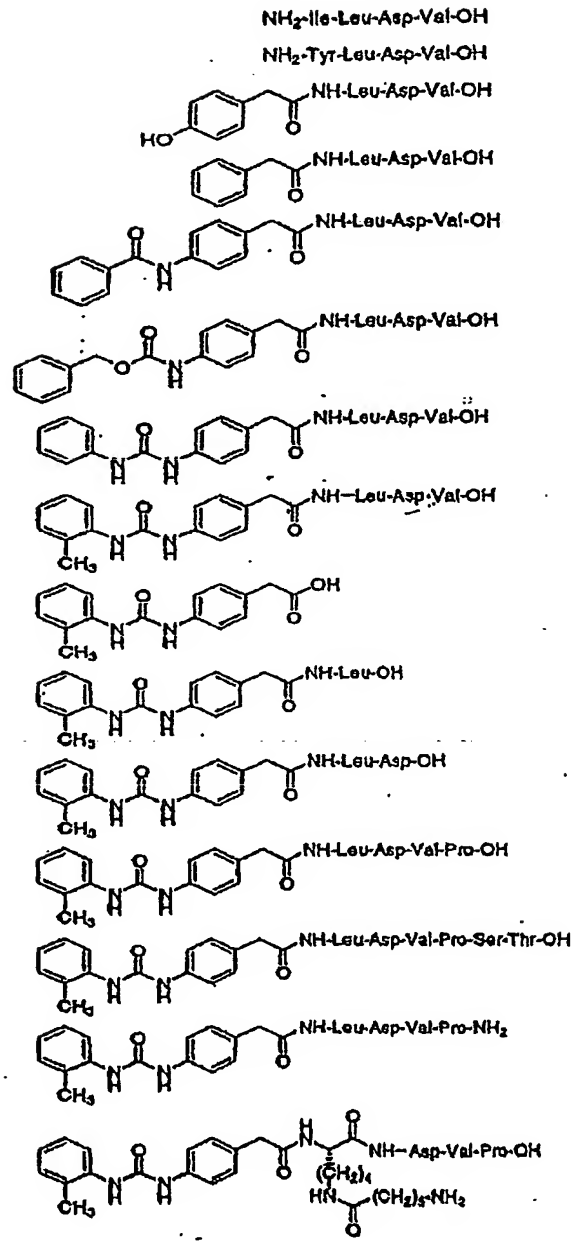
Fig. 5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NH2-Tyr-Leu-Asp-Val-OH
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NH-Leu-Asp-Val-OH
NH-Leu-Asp-Val-OH
NH-Leu-Asp-Val-OH
NH-Leu-Asp-Val-OH
NH—Leu-Asp-Val-OH
CH3
OH
NH-Leu-OH
NH-Leu-Asp-OH
NH-Leu-Asp-Val-Pro-OH
NH-Leu-Asp-Val-Pro-Ser-Thr-OH
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NH—Asp-Val-Pro-OH
(CH2)4
HN
(CH2)5-NH2

Fig. 6

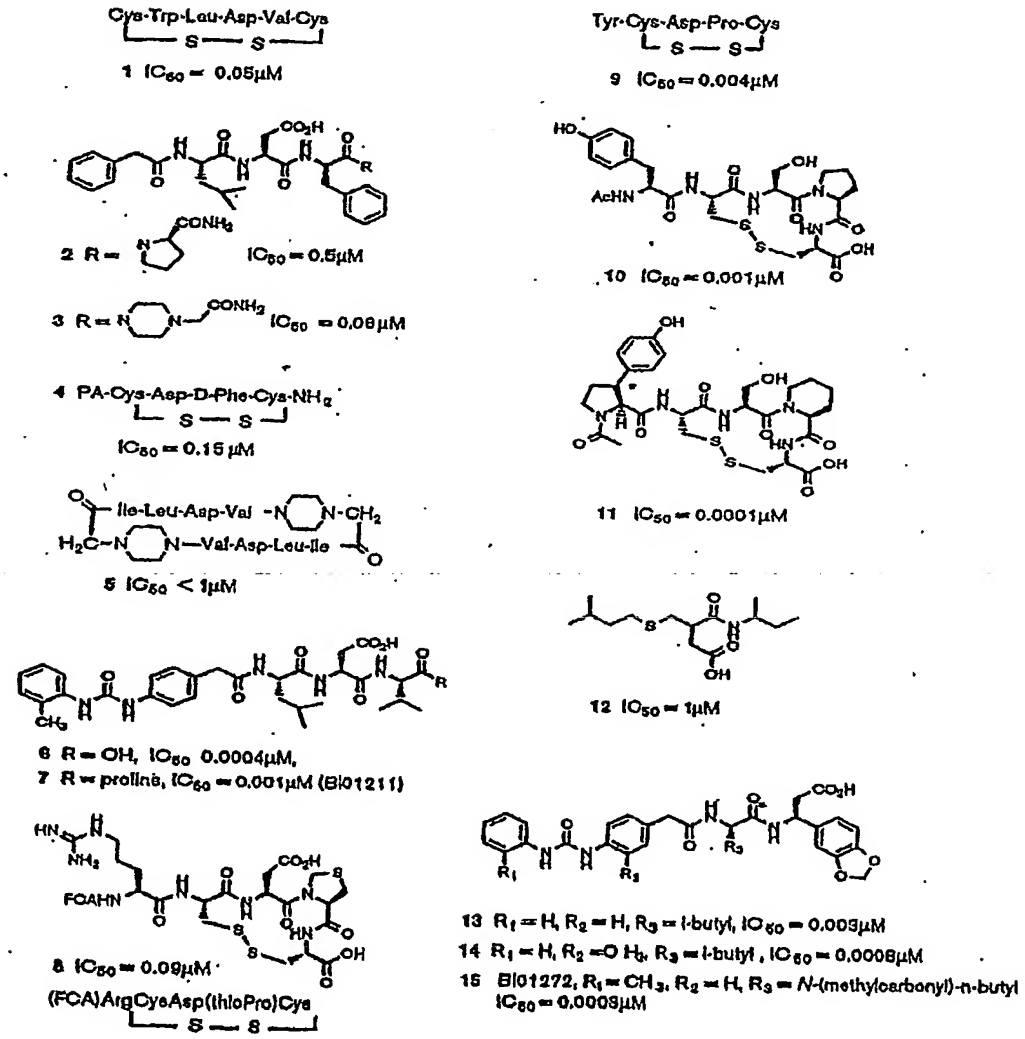
Cys-Trp-Leu-Asp-Val-Cys
1 IC50 = 0.05μM
Tyr-Cys-Asp-Pro-Cys
9 IC50 = 0.004μM
2 R = IC50 = 0.5μM
10 IC50 = 0.001μM
3 R = IC50 = 0.08μM
4 PA-Cys-Asp-D-Phe-Cys-NH2
IC50 = 0.15 μM
11 IC50 = 0.0001μM
Ile-Leu-Asp-Val
Val-Asp-Leu-Ile
5 IC50 < 1μM
12 IC50 = 1μM
6 R = OH, IC50 0.0004μM,
7 R = proline, IC50 = 0.001μM (BI01211)
13 R1 = H, R2 = H, R3 = t-butyl, IC50 = 0.003μM
14 R1 = H, R2 = O H3, R3 = t-butyl , IC50 = 0.0008μM
15 BI01272, R1 = CH3, R2 = H, R3 = N-(methylcarbonyl)-n-butyl
IC50 = 0.0009μM
8 IC50 = 0.09μM
(FCA)ArgCysAsp(thioPro)Cys

Fig. 7

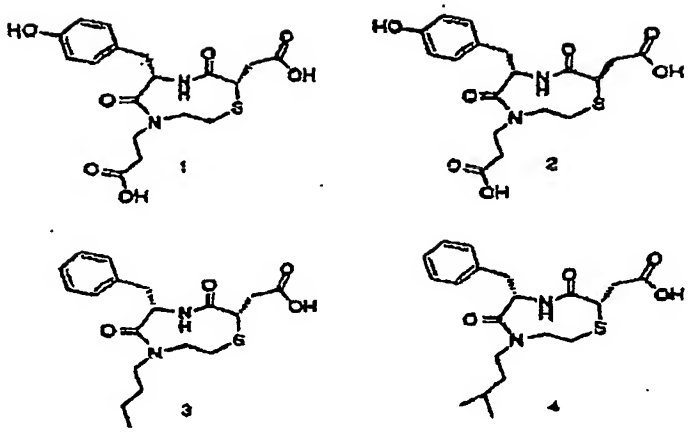

Fig. 8A

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Fig. 8B

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Fig. 9A

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Fig. 9B

2521 ctgtgaagtc acagataact ctggcgtggt acaacttgac tgcagtattg gctatatata
2581 tgtagatcat ctctcaagga tagatattag ctttctcctg gatgtgagct cactcagcag
2641 agcggaagag gacctcagta tcacagtgca tgctacctgt gaaaatgaag aggaaatgga
2701 caatctaaag cacagcagag tgactgtagc aataccttta aaatatgagg ttaagctgac
2761 tgttcatggg tttgtaaacc caacttcatt tgtgtatgga tcaaatgatg aaaatgagcc
2821 tgaaacgtgc atggtggaga aaatgaactt aactttccat gttatcaaca ctggcaatag
2881 tatggctccc aatgttagtg tggaaataat ggtaccaaat tcttttagcc cccaaactga
2941 taagctgttc aacattttgg atgtccagac tactactgga gaatgccact ttgaaaatta
3001 tcaaagagtg tgtgcattag agcagcaaaa gagtgcaatg cagaccttga aaggcatagt
3061 ccggttcttg tccaagactg ataagaggct attgtactgc ataaaagctg atccacattg
3121 tttaaatttc ttgtgtaatt ttgggaaaat ggaaagtgga aaagaagcca gtgttcatat
3181 ccaactggaa ggccggccat ccattttaga aatggatgag acttcagcac tcaagtttga
3241 aataagagca acaggttttc cagagccaaa tccaagagta attgaactaa acaaggatga
3301 gaatgttgcg catgttctac tggaaggact acatcatcaa agacccaaac gttatttcac
3361 catagtgatt atttcaagta gcttgctact tggacttatt gtacttctat tgatctcata
3421 tgttatgtgg aaggctggct tctttaaaag acaatacaaa tctatcctac aagaagaaaa
3481 cagaagagac agttggagtt atatcaacag taaaagcaat gatgattaag gacttctttc
3541 aaattgagag aatggaaaac ag

Fig. 10A

1 gtccgccaaa acctgcgcgg atagggaaga acagcacccc ggcgccgatt gccgtaccaa
61 acaagcctaa cgtccgctgg gccccggacg ccgcgcggaa aagatgaatt tacaaccaat
121 tttctggatt ggactgatca gttcagtttg ctgtgtgttt gctcaaacag atgaaaatag
181 atgtttaaaa gcaaatgcca aatcatgtgg agaatgtata caagcagggc caaattgtgg
241 gtggtgcaca aattcaacat ttttacagga aggaatgcct acttctgcac gatgtgatga
301 tttagaagcc ttaaaaaaga agggttgccc tccagatgac atagaaaatc ccagaggctc
361 caaagatata aagaaaaata aaaatgtaac caaccgtagc aaaggaacag cagagaagct
421 caagccagag gatattcatc agatccaacc acagcagttg gttttgcgat taagatcagg
481 ggagccacag acatttacat taaaattcaa gagagctgaa gactatccca ttgacctcta
541 ctaccttatg gacctgtctt attcaatgaa agacgatttg gagaatgtaa aaagtcttgg
601 aacagatctg atgaatgaaa tgaggaggat tacttcggac ttcagaattg gatttggctc
661 atttgtggaa aagactgtga tgccttacat tagcacaaca ccagctaagc tcaggaaccc
721 ttgcacaagt gaacagaact gcaccaccca atttagctac aaaaatgtgc tcagtcttac
781 taataaagga gaagtattta atgaacttgt tggaaaacag cgcatatctg gaaatttgga
841 ttctccagaa ggtggtttcg atgccatcat gcaagttgca gtttgtggat cactgattgg
901 ctggaggaat gttacacggc tgctggtgtt ttccacagat gccgggtttc actttgctgg
961 agatgggaaa cttggtggca ttgttttacc aaatgatgga caatgtcacc tggaaaataa
1021 tatgtacaca atgagccatt attatgatta tccttctatt gctcaccttg tccagaaact
1081 gagtgaaaat aatattcaga caatttttgc agttactgaa gaatttcagc ctgtttacaa
1141 ggagctgaaa aacttgatcc ctaagtcagc agtaggaaca ttatctgcaa attctagcaa
1201 tgtaattcag ttgatcattg atgcatacaa ttccctttcc tcagaagtca ttttggaaaa
1261 cggcaaattg tcagaaggag taacaataag ttacaaatct tactgcaaga acggggtgaa
1321 tggaacaggg gaaaatggaa gaaaatgttc caatatttcc attggagatg aggttcaatt
1381 tgaaattagc ataacttcaa ataagtgtcc aaaaaaggat tctgacagct ttaaaattag
1441 gcctctgggc tttacggagg aagtagaggt tattcttcag tacatctgtg aatgtgaatg
1501 ccaaagcgaa ggcatccctg aaagtcccaa gtgtcatgaa ggaaatggga catttgagtg
1561 tggcgcgtgc aggtgcaatg aagggcgtgt tggtagacat tgtgaatgca gcacagatga
1621 agttaacagt gaagacatgg atgcttactg caggaaagaa aacagttcag aaatctgcag
1681 taacaatgga gagtgcgtct gcggacagtg tgtttgtagg aagagggata atacaaatga
1741 aatttattct ggcaaattct gcgagtgtga taatttcaac tgtgatagat ccaatggctt
1801 aatttgtgga ggaaatggtg tttgcaagtg tcgtgtgtgt gagtgcaacc ccaactacac
1861 tggcagtgca tgtgactgtt ctttggatac tagtacttgt gaagccagca acggacagat
1921 ctgcaatggc cggggcatct gcgagtgtgg tgtctgtaag tgtacagatc cgaagtttca
1981 agggcaaacg tgtgagatgt gtcagacctg ccttggtgtc tgtgctgagc ataaagaatg
2041 tgttcagtgc agagccttca ataaaggaga aaagaaagac acatgcacac aggaatgttc
2101 ctattttaac attaccaagg tagaaagtcg ggacaaatta ccccagccgg tccaacctga
2161 tcctgtgtcc cattgtaagg agaaggatgt tgacgactgt tggttctatt ttacgtattc
2221 agtgaatggg aacaacgagg tcatggttca tgttgtggag aatccagagt gtcccactgg
2281 tccagacatc attccaattg tagctggtgt ggttgctgga attgttctta ttggccttgc
2341 attactgctg atatggaagc ttttaatgat aattcatgac agaagggagt ttgctaaatt
2401 tgaaaaggag aaaatgaatg ccaaatggga cacgggtgaa aatcctattt ataagagtgc

Fig. 10B

2461 cgtaacaact gtggtcaatc cgaagtatga gggaaaatga gtactgcccg tgcaaatccc
2521 acaacactga atgcaaagta gcaatttcca tagtcacagt taggtagctt tagggcaata
2581 ttgccatggt tttactcatg tgcaggtttt gaaaatgtac aatatgtata atttttaaaa
2641 tgttttatta ttttgaaaat aatgttgtaa ttcatgccag ggactgacaa aagacttgag
2701 acaggatggt tattcttgtc agctaaggtc acattgtgcc tttttgacct tttcttcctg
2761 gactattgaa atcaagctta ttggattaag tgatatttct atagcgattg aaagggcaat
2821 agttaaagta atgagcatga tgagagtttc tgttaatcat gtattaaaac tgatttttag
2881 ctttacatat gtcagtttgc agttatgcag aatccaaagt aaatgtcctg ctagctagtt
2941 aaggattgtt ttaaatctgt tattttgcta tttgcctgtt agacatgact gatgacatat
3001 ctgaaagaca agtatgttga gagttgctgg tgtaaaatac gtttgaaata gttgatctac
3061 aaaggccatg ggaaaaattc agagagttag gaaggaaaaa ccaatagctt taaaacctgt
3121 gtgccatttt aagagttact taatgtttgg taacttttat gccttcactt tacaaattca
3181 agccttagat aaaagaaccg agcaattttc tgctaaaaag tccttgattt agcactattt
3241 acatacaggc catactttac aaagtatttg ctgaatgggg acctttgag ttgaatttat
3301 tttattattt ttattttgtt taatgtctgg tgctttctat cacctcttct aatcttttaa
3361 tgtatttgtt tgcaattttg gggtaagact tttttatgag tacttttttct ttgaagtttt
3421 agcggtcaat ttgccttttt aatgaacatg tgaagttata ctgtggctat gcaacagctc
3481 tcacctacgc gagtcttact ttgagttagt gccataacag accactgtat gtttacttct
3541 caccatttga gttgcccatc ttgtttcaca ctagtcacat tcttgtttta agtgccttta
3601 gttttaacag ttca

Fig. 11

1 atgcctggga agatggtcgt gatccttgga gcctcaaata tactttggat aatgtttgca
61 gcttctcaag cttttaaaat cgagaccacc ccagaatcta gatatcttgc tcagattggt
121 gactccgtct cattgacttg cagcaccaca ggctgtgagt ccccattttt ctcttggaga
181 acccagatag atagtccact gaatgggaag gtgacgaatg aggggaccac atctacgctg
241 acaatgaatc ctgttagttt tgggaacgaa cactcttacc tgtgcacagc aacttgtgaa
301 tctaggaaat tggaaaaagg aatccaggtg gagatctact cttttcctaa ggatccagag
361 attcatttga gtggccctct ggaggctggg aagccgatca cagtcaagtg ttcagttgct
421 gatgtatacc catttgacag gctggagata gacttactga aaggagatca tctcatgaag
481 agtcaggaat ttctggagga tgcagacagg aagtccctgg aaaccaagag tttggaagta
541 acctttactc ctgtcattga ggatattgga aaagttcttg tttgccgagc taaattacac
601 attgatgaaa tggattctgt gcccacagta aggcaggctg taaaagaatt gcaagtctac
661 atatcaccca agaatacagt tatttctgtg aatccatcca caaagctgca agaaggtggc
721 tctgtgacca tgacctgttc cagcgagggt ctaccagctc cagagatttt ctggagtaag
781 aaattagata atgggaatct acagcacctt tctggaaatg caactctcac cttaattgct
841 atgaggatgg aagattctgg aatttatgtg tgtgaaggag ttaatttgat tgggaaaaac
901 agaaaagagg tggaattaat tgttcaagag aaaccattta ctgttgagat ctcccctgga
961 ccccggattg ctgctcagat tggagactca gtcatgttga catgtagtgt catgggctgt
1021 gaatccccat ctttctcctg gagaacccag atagacagcc ctctgagcgg gaaggtgagg
1081 agtgagggga ccaattccac gctgaccctg agccctgtga gttttgagaa cgaacactct
1141 tatctgtgca cagtgacttg tggacataag aaactggaaa agggaatcca ggtggagctc
1201 tactcattcc ctagagatcc agaaatcgag atgagtggtg gcctcgtgaa tgggagctct
1261 gtcactgtaa gctgcaaggt tcctagcgtg taccccccttg accggctgga gattgaatta
1321 cttaaggggg agactattct ggagaatata gagttttgg aggatacgga tatgaaatct
1381 ctagagaaca aaagtttgga aatgaccttc atccctacca ttgaagatac tggaaaagct
1441 cttgtttgtc aggctaagtt acatattgat gacatggaat tcgaacccaa acaaaggcag
1501 agtacgcaaa cactttatgt caatgttgcc cccagagata caaccgtctt ggtcagccct
1561 tcctccatcc tggaggaagg cagttctgtg aatatgacat gcttgagcca gggctttcct
1621 gctccgaaaa tcctgtggag caggcagctc cctaacgggg agctacagcc tctttctgag
1681 aatgcaactc tcaccttaat ttctacaaaa atggaagatt ctggggttta tttatgtgaa
1741 ggaattaacc aggctggaag aagcagaaag gaagtggaat taattatcca agttactcca
1801 aaagacataa aacttacagc ttttccttct gagagtgtca aagaaggaga cactgtcatc
1861 atctcttgta catgtggaaa tgttccagaa acatggataa tcctgaagaa aaaagcggag
1921 acaggagaca cagtactaaa atctatagat ggcgcctata ccatccgaaa ggcccagttg
1981 aaggatgcgg gagtatatga atgtgaatct aaaaacaaag ttggctcaca attaagaagt
2041 ttaacacttg atgttcaagg aagagaaaac aacaaagact attttctcc tgagcttctc
2101 gtgctctatt ttgcatcctc cttaataata cctgccattg gaatgataat ttactttgca
2161 agaaaagcca acatgaaggg gtcatatagt cttgtagaag cacagaaatc aaaagtgtag

Fig. 12A

1 gaagagcaag aggcaggctc agcaaatggt tcagccccag tccccggtgg ctgtcagtca
61 aagcaagccc ggttgttatg acaatggaaa acactatcag ataaatcaac agtgggagcg
121 gacctaccta ggtaatgtgt tggtttgtac ttgttatgga ggaagccgag gttttaactg
181 cgaaagtaaa cctgaagctg aagagacttg ctttgacaag tacactggga acacttaccg
241 agtgggtgac acttatgagc gtcctaaaga ctccatgatc tgggactgta cctgcatcgg
301 ggctgggcga gggagaataa gctgtaccat cgcaaaccgc tgccatgaag ggggtcagtc
361 ctacaagatt ggtgacacct ggaggagacc acatgagact ggtggttaca tgttagagtg
421 tgtgtgtctt ggtaatggaa aaggagaatg gacctgcaag cccatagctg agaagtgttt
481 tgatcatgct gctgggactt cctatgtggt cggagaaacg tgggagaagc cctaccaagg
541 ctggatgatg gtagattgta cttgcctggg agaaggcagc ggacgcatca cttgcacttc
601 tagaaataga tgcaacgatc aggacacaag gacatcctat agaattggag acacctggag
661 caagaaggat aatcgaggaa acctgctcca gtgcatctgc acaggcaacg gccgaggaga
721 gtggaagtgt gagaggcaca cctctgtgca gaccacatcg agcggatctg gccccttcac
781 cgatgttcgt gcagctgttt accaaccgca gcctcacccc cagcctcctc cctatggcca
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901 aaataagcaa atgctttgca cgtgcctggg caacggagtc agctgccaag agacagctgt
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1021 tggcaggacg ttctactcct gcaccacgga agggcgacag gacggacatc tttggtgcag
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1141 ggttcagact caaggaggaa attccaatgg tgccttgtgc cacttcccct tcctatacaa
1201 caaccacaat tacactgatt gcacttctga gggcagaaga gacaacatga agtggtgtgg
1261 gaccacacag aactatgatg ccgaccagaa gtttgggttc tgccccatgg ctgcccacga
1321 ggaaatctgc acaaccaatg aaggggtcat gtaccgcatt ggagatcagt gggataagca
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1621 gacgttttat caaattggag attcatggga gaagtatgtg catggtgtca gataccagtg
1681 ctactgctat ggccgtggca ttggggagtg gcattgccaa cctttacaga cctatccaag
1741 ctcaagtggt cctgtcgaag tatttatcac tgagactccg agtcagccca actcccaccc
1801 catccagtgg aatgcaccac agccatctca catttccaag tacattctca ggtggagacc
1861 taaaaattct gtaggccgtt ggaaggaagc taccatacca ggccacttaa actcctacac
1921 catcaaaggc ctgaagcctg gtgtggtata cgagggccag ctcatcagca tccagcagta
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2281 tgtaaatgtc tatcagatat ctgaggatgg ggagcagagt ttgatcctgt ctacttcaca
2341 aacaacagcg cctgatgccc ctcctgaccc gactgtggac caagttgatg acacctcaat
2401 tgttgttcgc tggagcagac cccaggctcc catcacaggg tacagaatag tctattcgcc
2461 atcagtagaa ggtagcagca cagaactcaa ccttcctgaa actgcaaact ccgtcaccct
2521 cagtgacttg caacctggtg ttcagtataa catcactatc tatgctgtgg aagaaaatca

Fig. 12B

2581 agaaagtaca cctgttgtca ttcaacaaga aaccactggc accccacgct cagatacagt
2641 gccctctccc agggacctgc agtttgtgga agtgacagac gtgaaggtca ccatcatgtg
2701 gacaccgcct gagagtgcag tgaccggcta ccgtgtggat gtgatccccg tcaacctgcc
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3421 aaacaaagtg gtgacaccat tgtctccacc aacaaacttg catctggagg caaaccctga
3481 cactggagtg ctcacagtct cctgggagag gagcaccacc ccagacatta ctggttatag
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3601 tgatcagagc tcctgcactt ttgataacct gagtcccggc ctggagtaca atgtcagtgt
3661 ttacactgtc aaggatgaca aggaaagtgt ccctatctct gataccatca tcccagctgt
3721 tcctcctccc actgacctgc gattcaccaa cattggtcca gacaccatgc gtgtcacctg
3781 ggctccaccc ccatccattg atttaaccaa cttcctggtg cgttactcac ctgtgaaaaa
3841 tgaggaagat gttgcagagt tgtcaatttc tccttcagac aatgcagtgg tcttaacaaa
3901 tctcctgcct ggtacagaat atgtagtgag tgtctccagt gtctacgaac aacatgagag
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4621 ccctgttact ggttacagag taaccaccac tcccaaaaat ggaccaggac caacaaaaac
4681 taaaactgca ggtccagatc aaacagaaat gactattgaa ggcttgcagc ccacagtgga
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4861 catcaaaatt gcttgggaaa gcccacaggg gcaagtttcc aggtacaggg tgacctactc
4921 gagccctgag gatggaatcc atgagctatt ccctgcacct gatggtgaag aagacactgc
4981 agagctgcaa ggcctcagac cgggttctga gtacacagtc agtgtggttg ccttgcacga
5041 tgatatggag agccagcccc tgattggaac ccagtccaca gctattcctg caccaactga

Fig. 12C

5101 cctgaagttc actcaggtca cacccacaag cctgagcgcc cagtggacac cacccaatgt
5161 tcagctcact ggatatcgag tgcgggtgac ccccaaggag aagaccggac caatgaaaga
5221 aatcaacctt gctcctgaca gctcatccgt ggttgtatca ggacttatgg tggccaccaa
5281 atatgaagtg agtgtctatg ctcttaagga cactttgaca agcagaccag ctcagggtgt
5341 tgtcaccact ctggagaatg tcagcccacc aagaagggct cgtgtgacag atgctactga
5401 gaccaccatc accattagct ggagaaccaa gactgagacg atcactggct tccaagttga
5461 tgccgttcca gccaatggcc agactccaat ccagagaacc atcaagccag atgtcagaag
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5581 tgacaatgct cggagctccc ctgtggtcat cgacgcctcc actgccattg atgcaccatc
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5761 ggtccctcgg ccccgccctg gtgtcacaga ggctactatt actggcctgg aaccgggaac
5821 cgaatataca atttatgtca ttgccctgaa gaataatcag aagagcgagc ccctgattgg
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6001 gtatgacact ggaaatggta ttcagcttcc tggcacttct ggtcagcaac ccagtgttgg
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6121 ccccataagg cataggccaa gaccataccc gccgaatgta ggacaagaag ctctctctca
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6241 tgttggcact gatgaagaac ccttacagtt cagggttcct ggaacttcta ccagtgccac
6301 tctgacaggc ctcaccagag gtgccaccta caacatcata gtggaggcac tgaaagacca
6361 gcagaggcat aaggttcggg aagaggttgt taccgtgggc aactctgtca acgaaggctt
6421 gaaccaacct acggatgact cgtgctttga ccctacaca gtttcccatt atgccgttgg
6481 agatgagtgg gaacgaatgt ctgaatcagg ctttaaactg ttgtgccagt gcttaggctt
6541 tggaagtggt catttcagat gtgattcatc tagatggtgc catgacaatg gtgtgaacta
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6721 tgggaagaca taccacgtag gagaacagtg gcagaaggaa tatctcggtg ccatttgctc
6781 ctgcacatgc tttggaggcc agcggggctg gcgctgtgac aactgccgca gacctggggg
6841 tgaacccagt cccgaaggca ctactggcca gtcctacaac cagtattctc agagatacca
6901 tcagagaaca aacactaatg ttaattgccc aattgagtgc ttcatgcctt tagatgtaca
6961 ggctgacaga gaagattccc gagagtaaat catctttcca atccagagga acaagcatgt
7021 ctctctgcca agatccatct aaactggagt gatgttagca gacccagctt agagttcttc
7081 tttctttctt aagccctttg ctctggagga agttctccag cttcagctca actcacagct
7141 tctccaagca tcaccctggg agtttcctga gggttttctc ataaatgagg gctgcacatt
7201 gcctgttctg cttcgaagta ttcaataccg ctcagtattt taaatgaagt gattctaaga
7261 tttggtttgg gatcaatagg aaagcatatg cagccaacca agatgcaaat gttttgaaat
7321 gatatgacca aaatttttag taggaaagtc acccaaacac ttctgctttc acttaagtgt
7381 ctggcccgca atactgtagg aacaagcatg atcttgttac tgtgatattt taaatatcca
7441 cagtactcac tttttccaaa tgatcctagt aattgcctag aaatatcttt ctcttacctg
7501 ttatttatca atttttccca gtatttttat acggaaaaaa ttgtattgaa aacacttagt
7561 atgcagttga taagaggaat ttggtataat tatggtgggt gattattttt tatactgtat
7621 gtgccaaagc tttactactg tggaaagaca actgttttaa taaaagattt acattccaca

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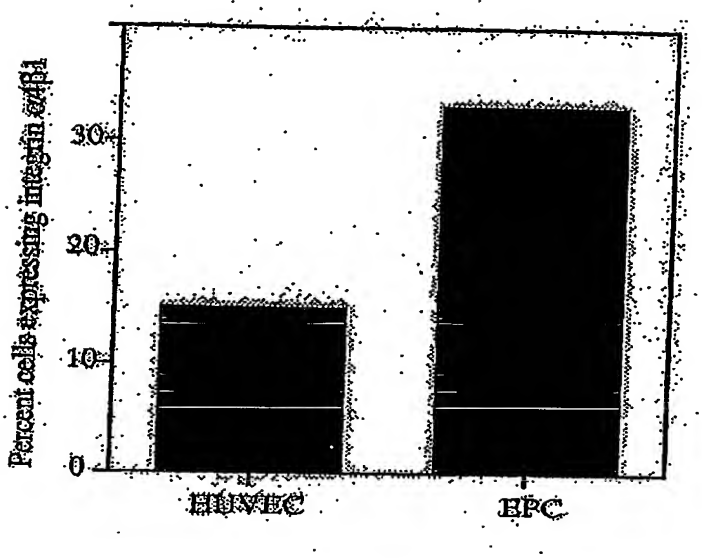

Fig. 13

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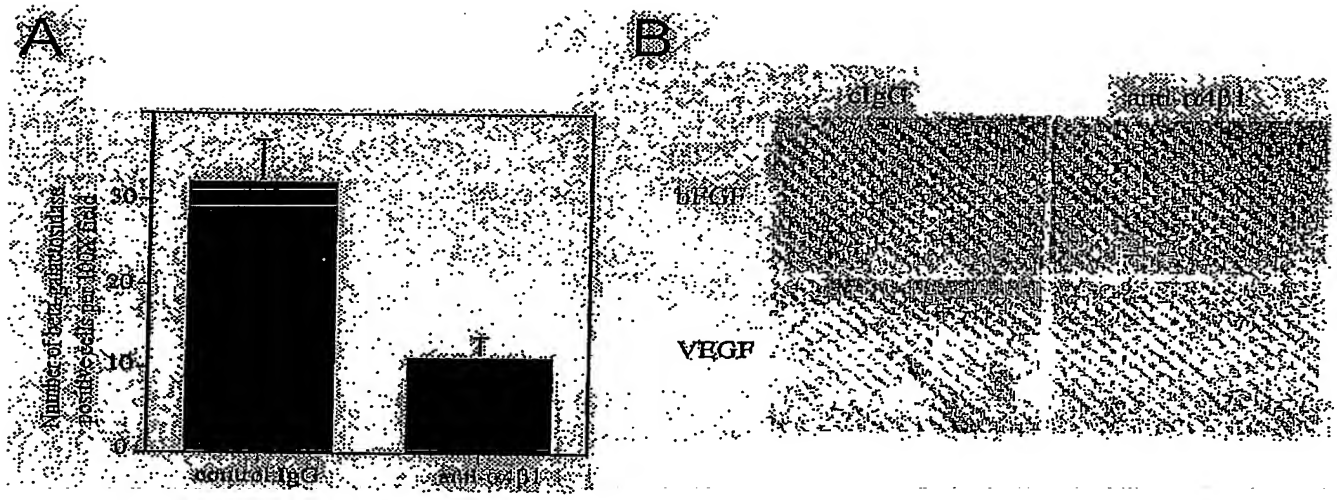
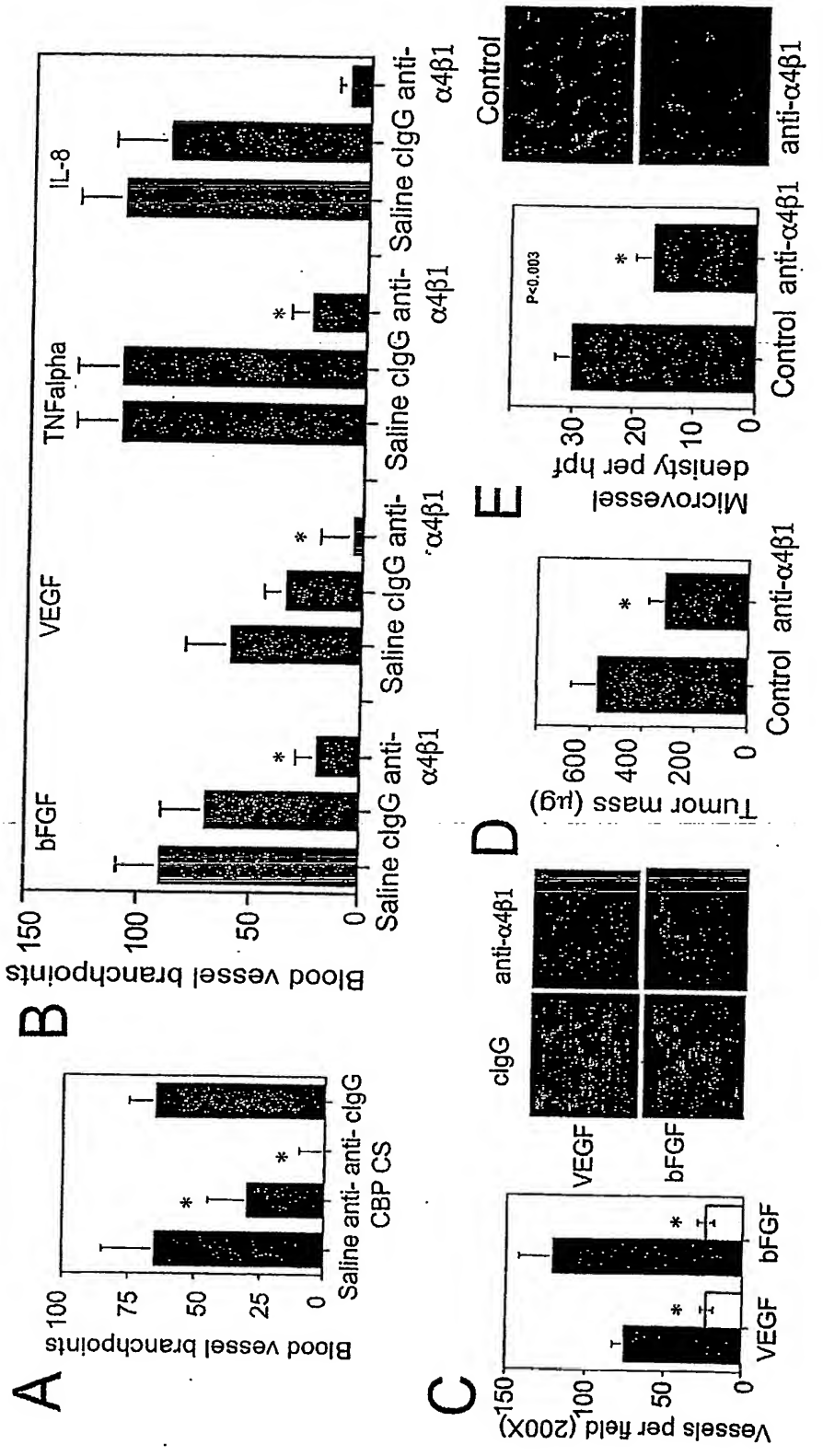


Fig. 14


A
Blood vessel branchpoints
100
75
50
25
0
Saline anti- anti- clgG
CBP CS
B
Blood vessel branchpoints
150
100
50
0
bFGF
VEGF
TNFalpha
IL-8
Saline clgG anti-α4β1
C
Vessels per field (200X)
150
100
50
0
VEGF
bFGF
clgG
anti-α4β1
D
Tumor mass (µg)
600
400
200
0
Control
anti-α4β1
E
Microvessel density per hpf
30
20
10
0
P<0.003
Control
anti-α4β1

Fig, 15

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Fig. 16

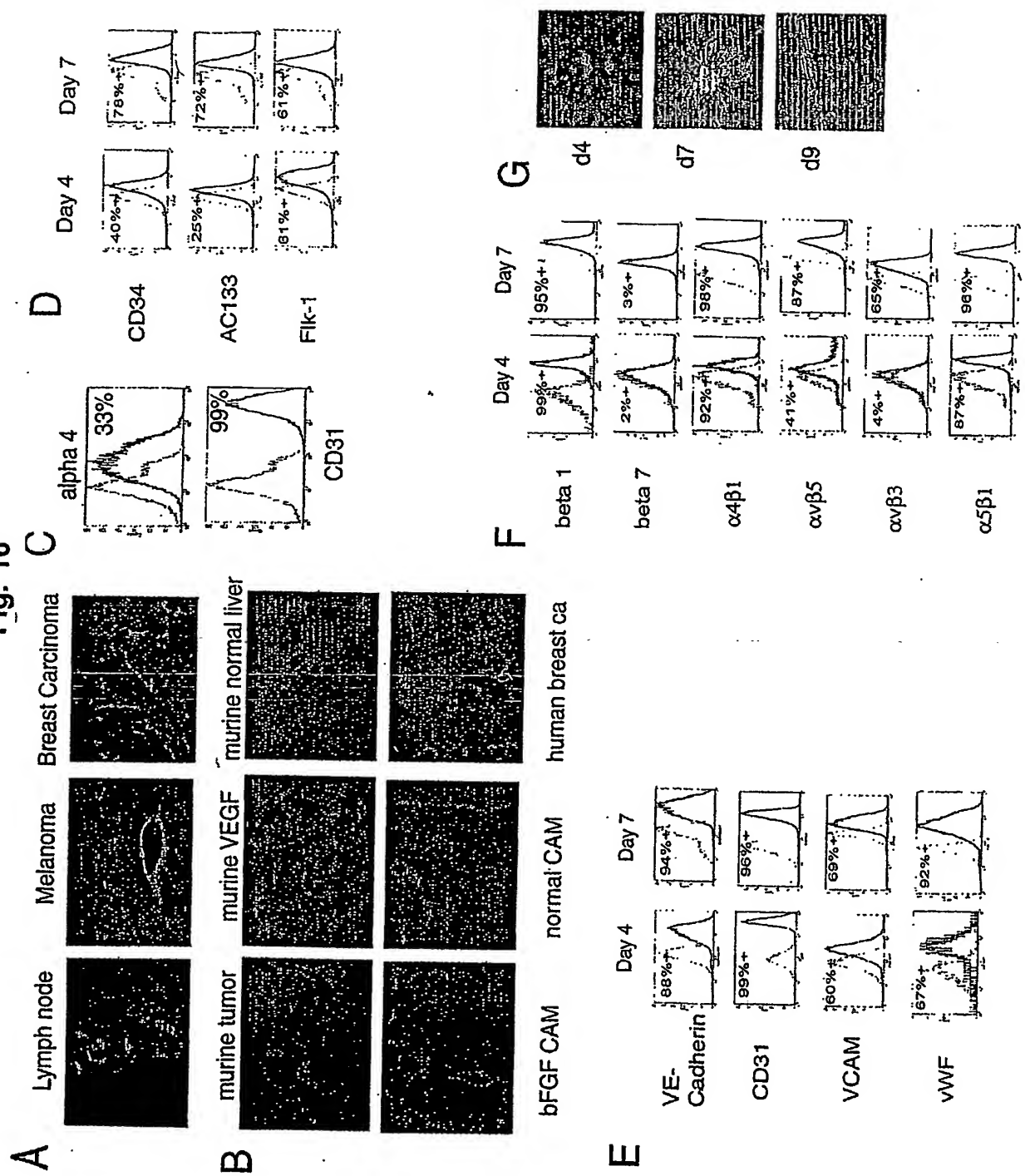

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Fig. 17

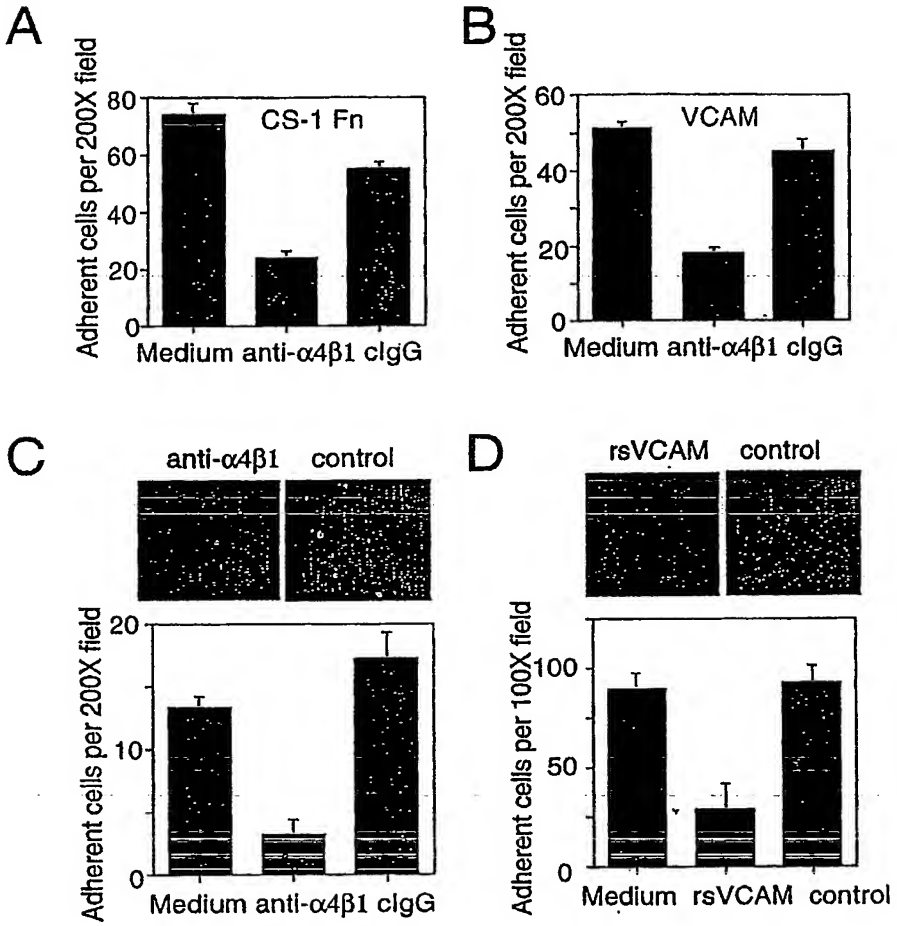

Fig. 18

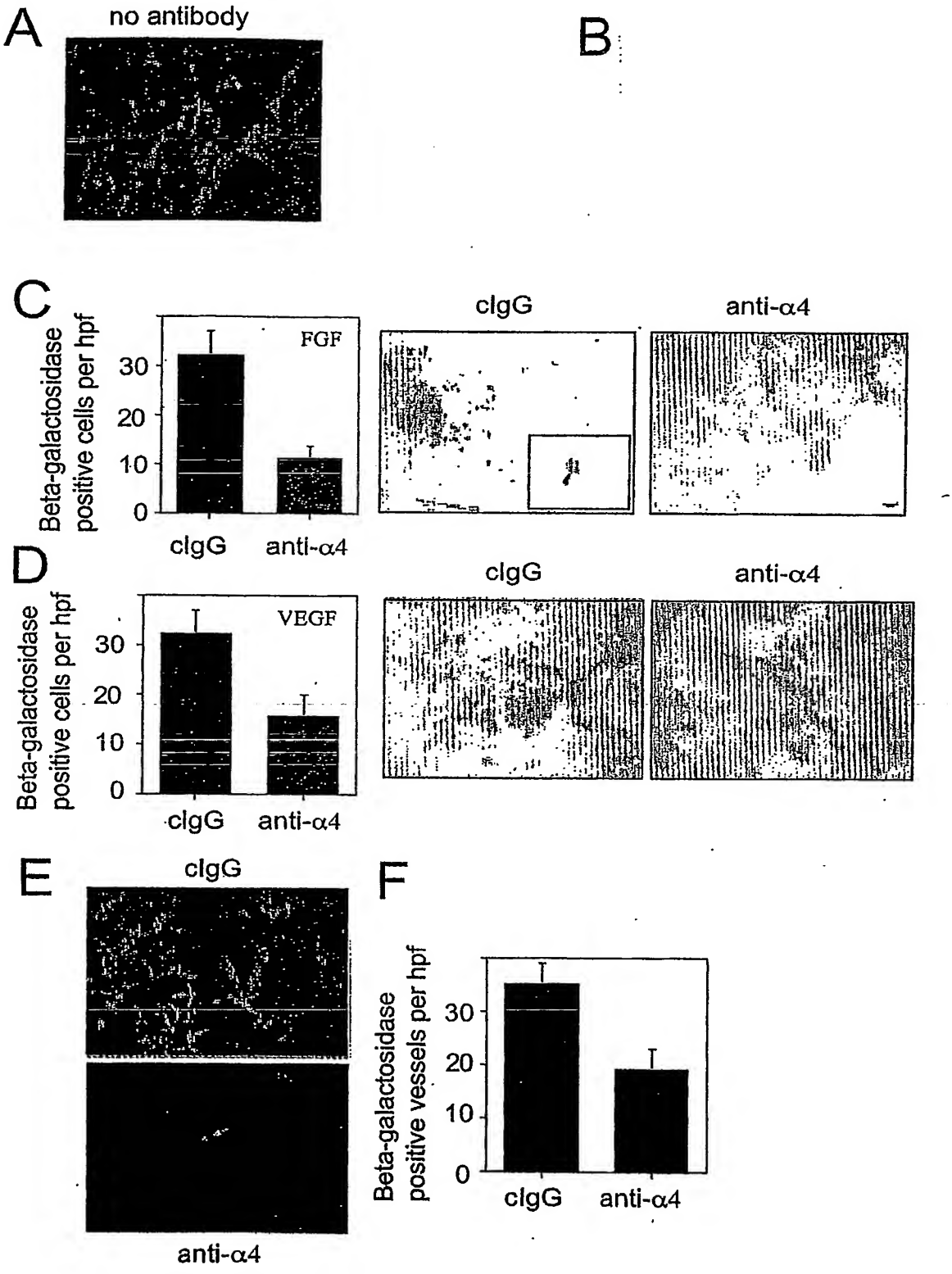
A
no antibody
B
C
Beta-galactosidase positive cells per hpf
FGF
30
20
10
0
cIgG
anti-α4
cIgG
anti-α4
D
Beta-galactosidase positive cells per hpf
VEGF
30
20
10
0
cIgG
anti-α4
cIgG
anti-α4
E
cIgG
anti-α4
F
Beta-galactosidase positive vessels per hpf
30
20
10
0
cIgG
anti-α4

Fig. 19

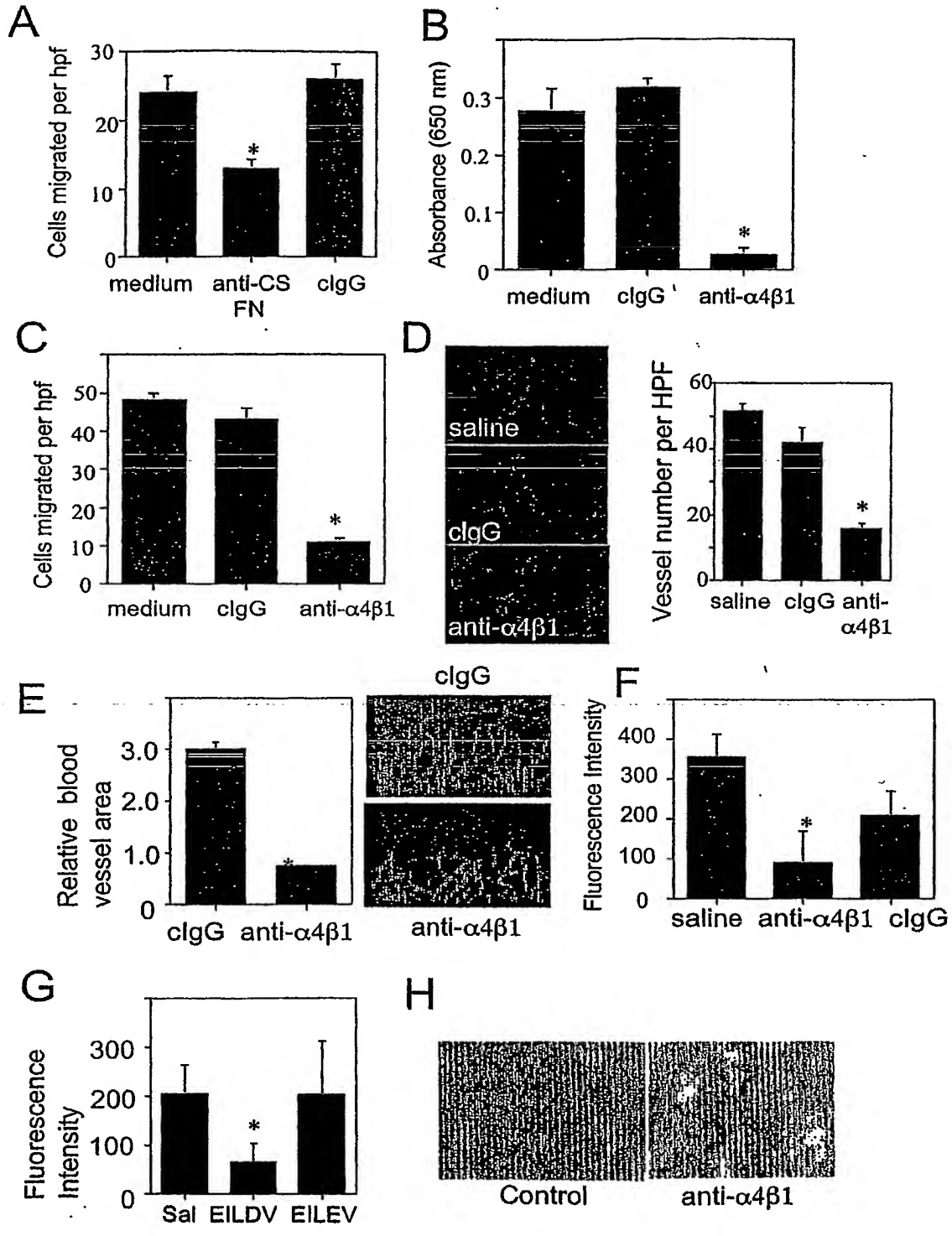
A
Cells migrated per hpf
30
20
10
0
*
medium
anti-CS FN
cIgG
B
Absorbance (650 nm)
0.3
0.2
0.1
0
*
medium
cIgG
anti-α4β1
C
Cells migrated per hpf
50
40
30
20
10
0
*
medium
cIgG
anti-α4β1
D
saline
cIgG
anti-α4β1
Vessel number per HPF
60
40
20
0
*
saline
cIgG
anti-α4β1
E
Relative blood vessel area
3.0
2.0
1.0
0
*
cIgG
anti-α4β1
cIgG
anti-α4β1
F
Fluorescence Intensity
400
300
200
100
0
*
saline
anti-α4β1
cIgG
G
Fluorescence Intensity
300
200
100
0
*
Sal
EILDV
EILEV
H
Control
anti-α4β1

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Fig. 20

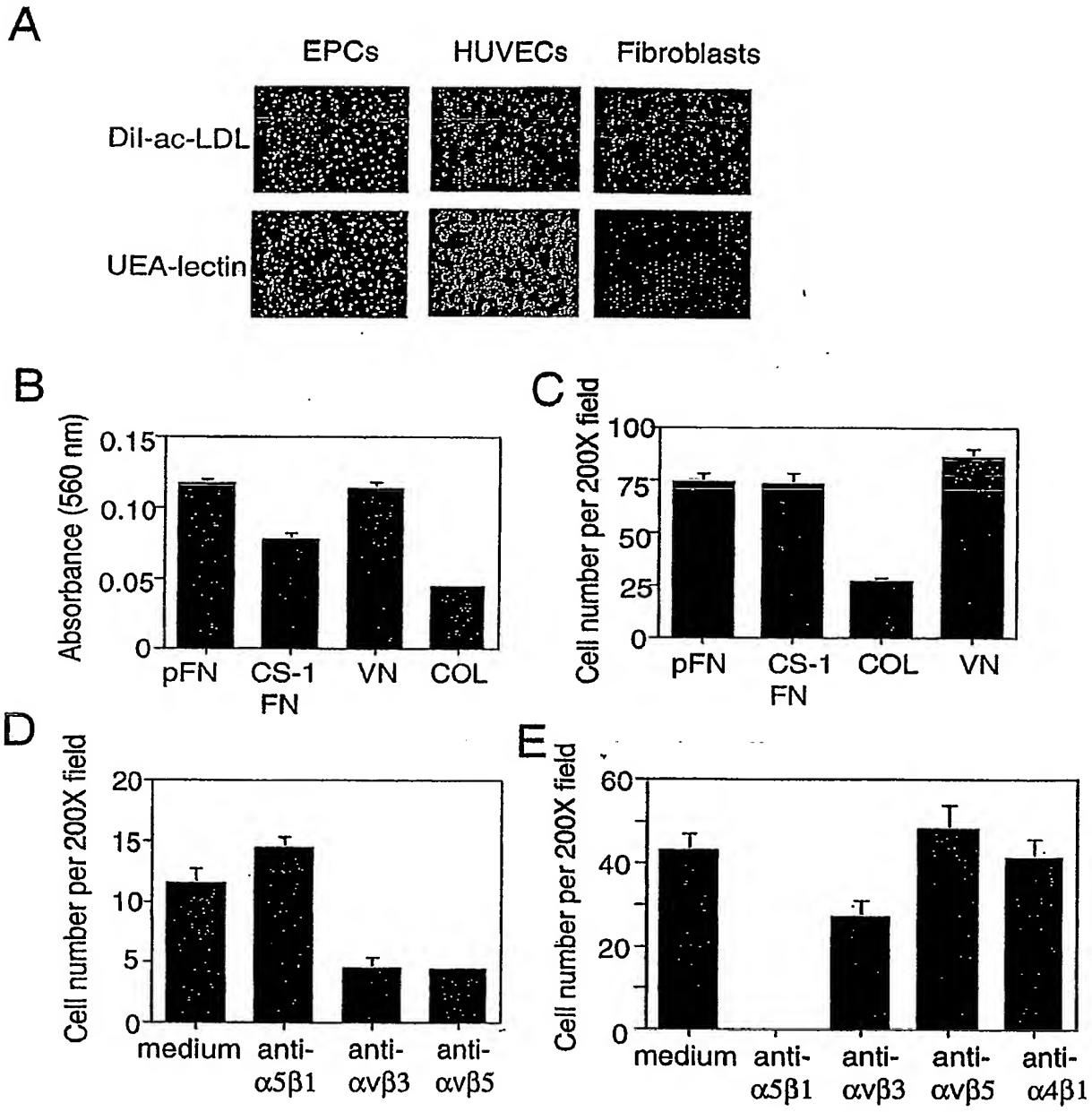

Fig. 21

Endothelial progenitor cells

Bone marrow derived cells that can differentiate into ECs

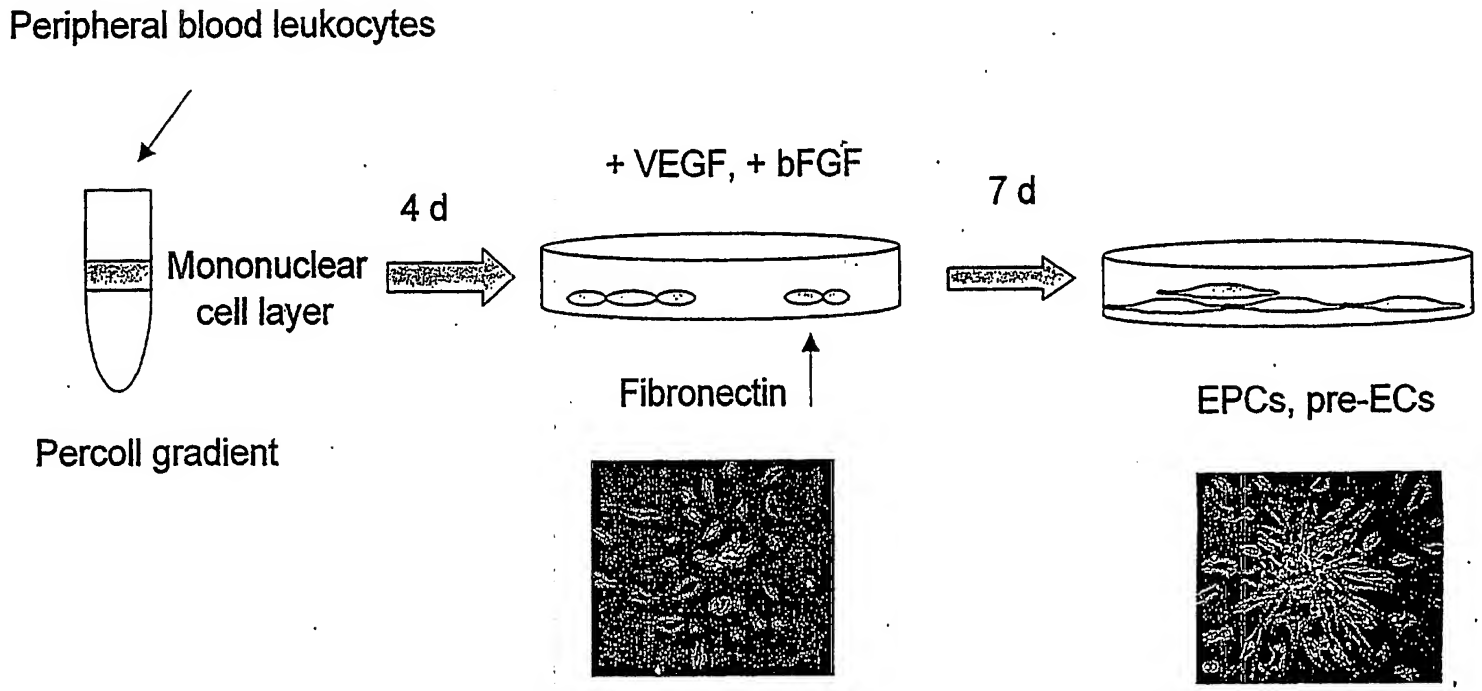

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Fig. 22

Integrin α4β1 appears to be an early marker of EPCs

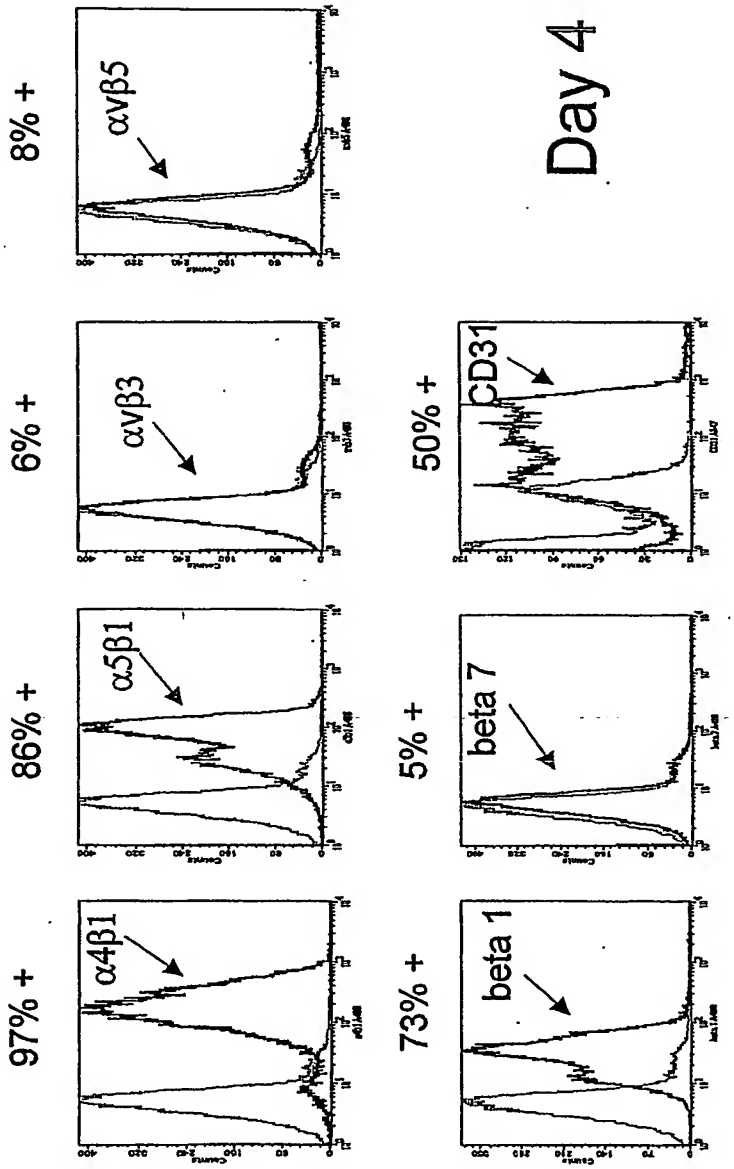

Fig. 23

EPC's remain α4β1 positive and acquire αv integrin expression

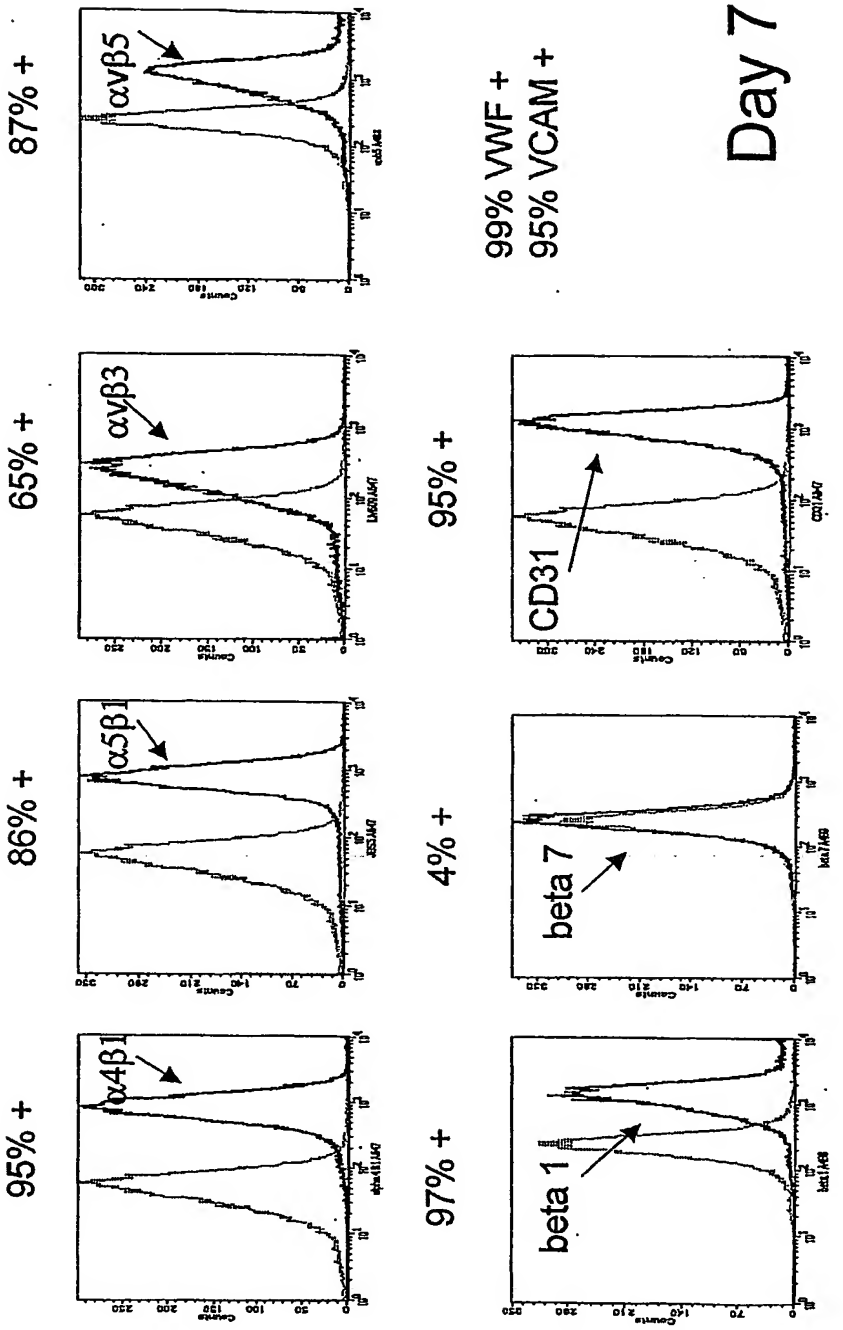

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Fig. 24

EPC maturation

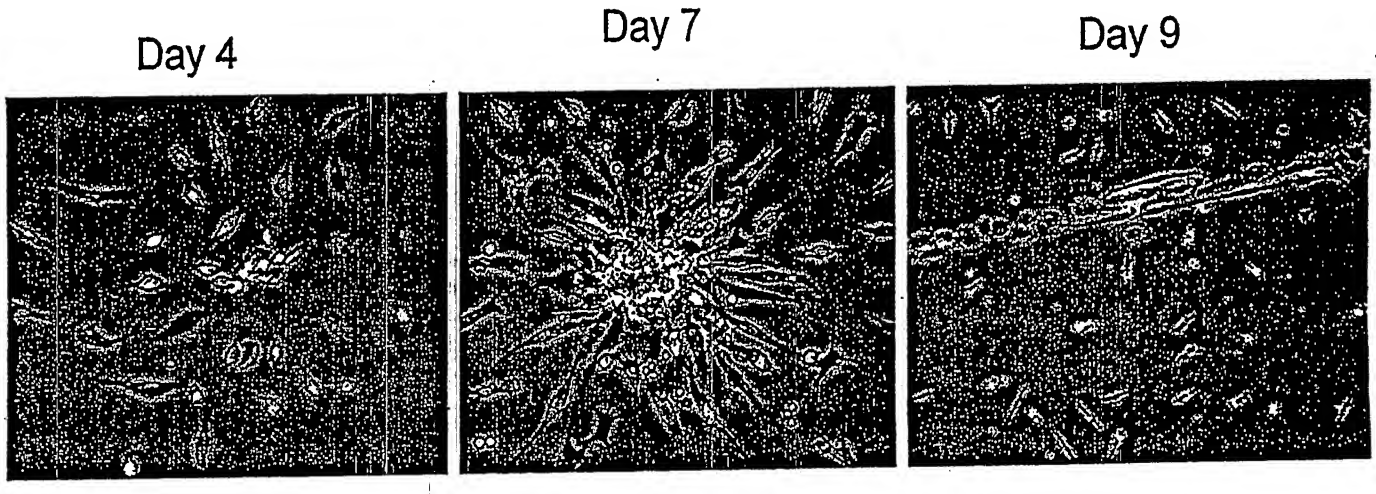

Fig. 25

α4β1 mediates EPC adhesion to CS-1 fibronectin

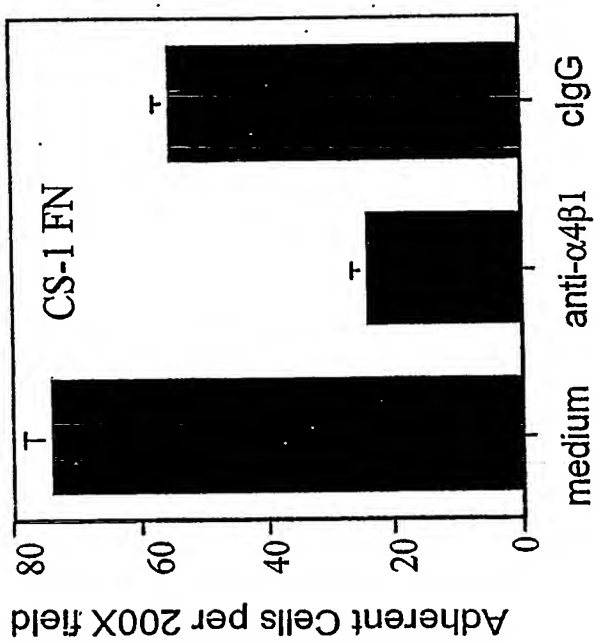

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Fig. 26

α4β1 mediates EPC adhesion to rsVCAM

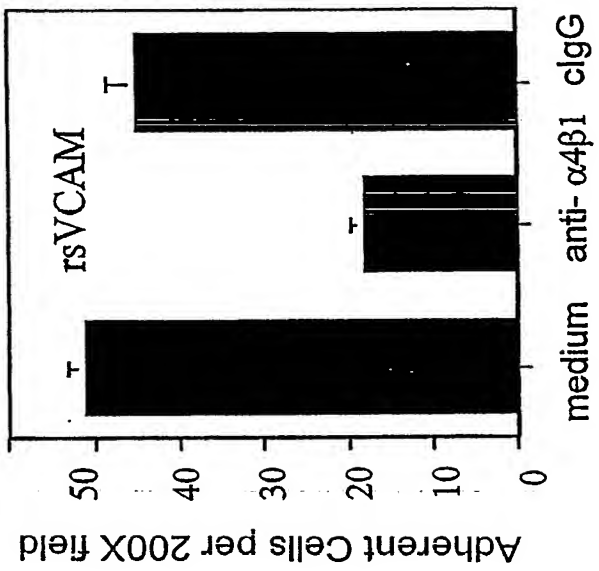
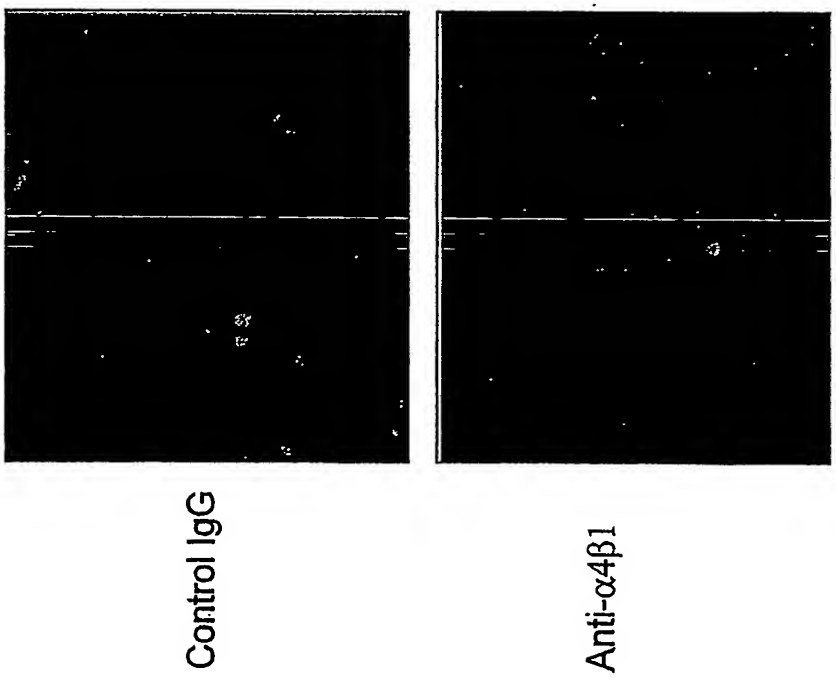


Fig. 27

EPCs adhere to endothelial monolayers via α4β1



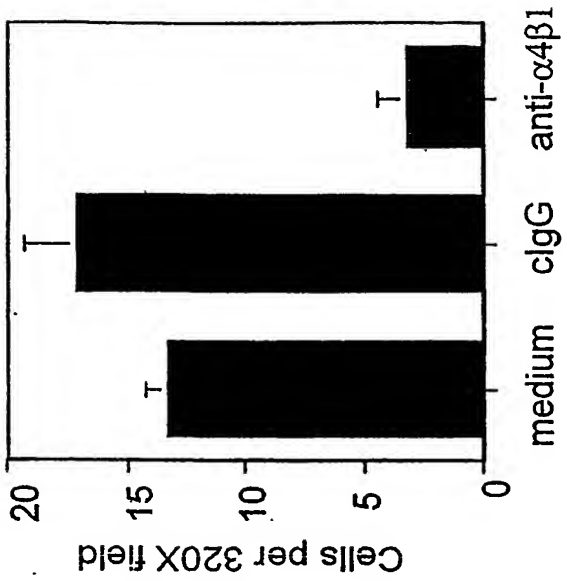


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Fig. 28

EPCs adhere to endothelial monolayers in a VCAM-dependent manner

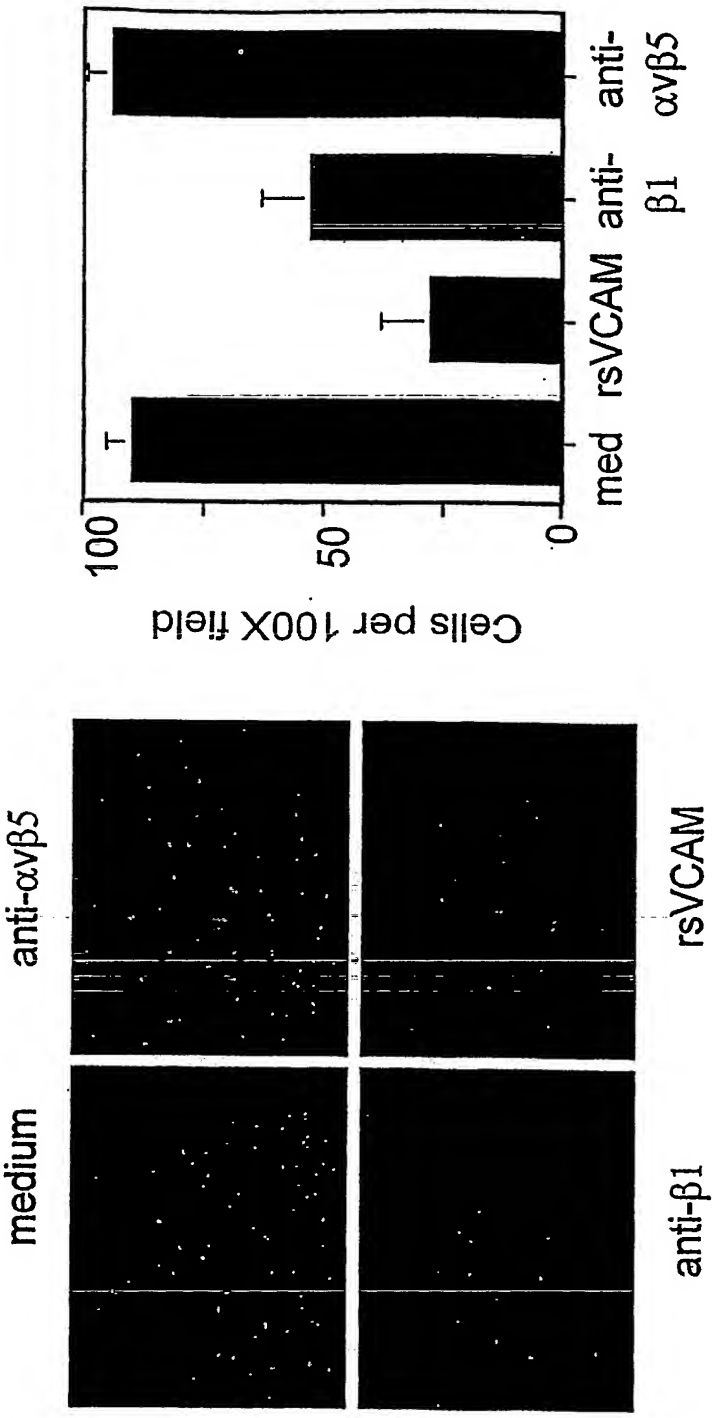

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Fig. 29

Tie2 BMT model of stem cell role in neovascularization

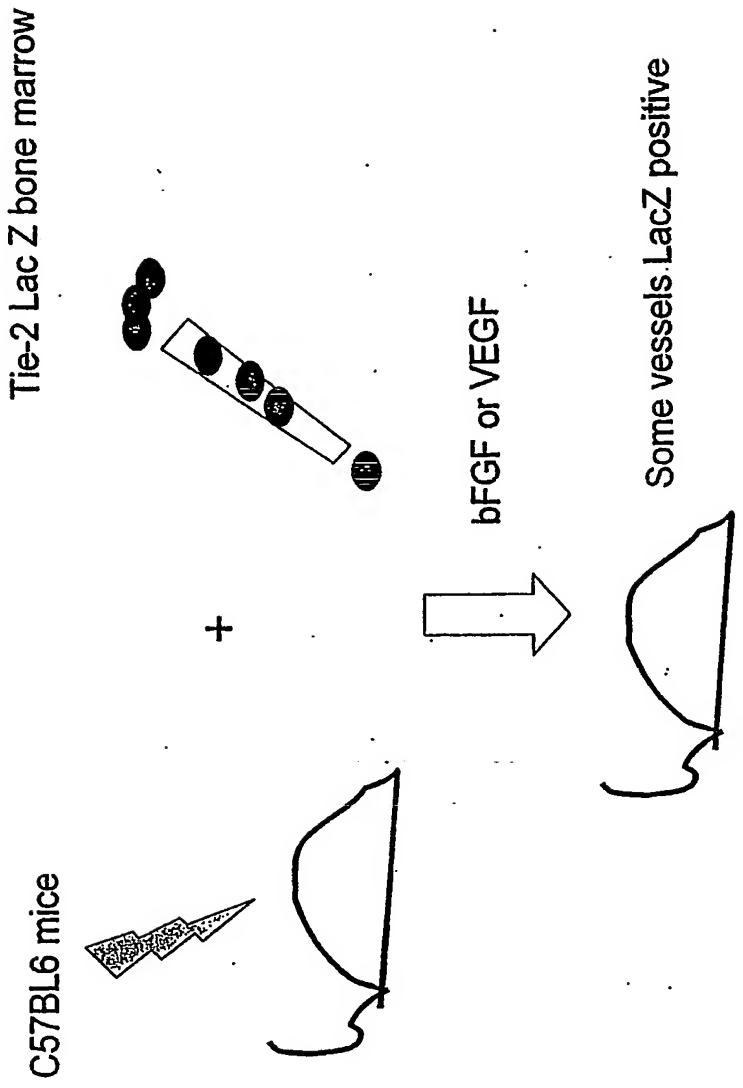

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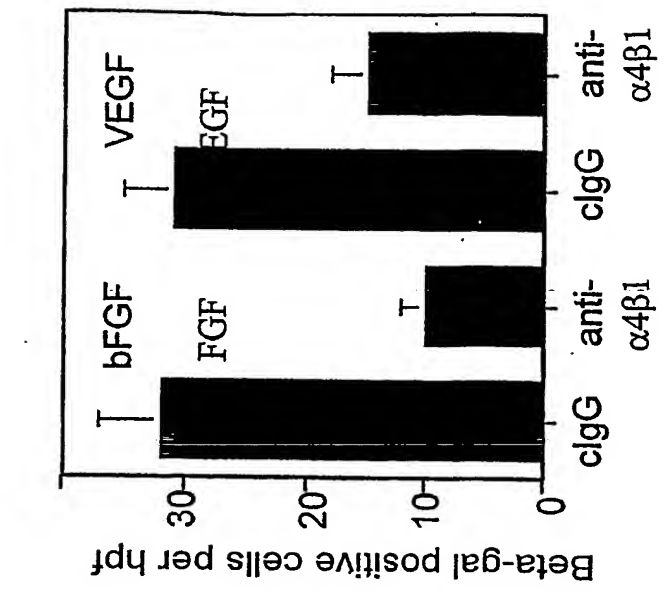
Fig. 30

Antagonists of α4β1 block EPC entry into neovascular beds



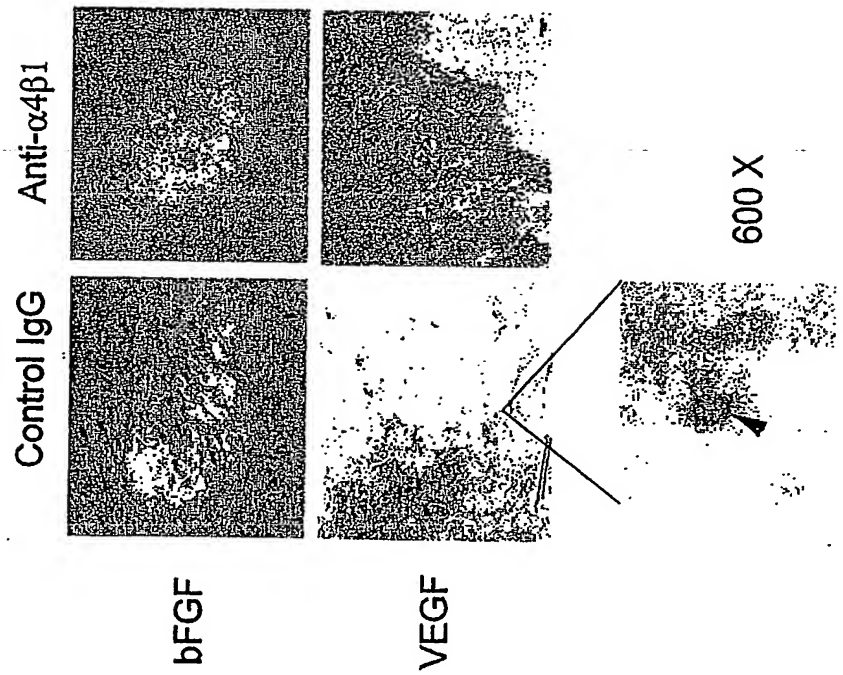


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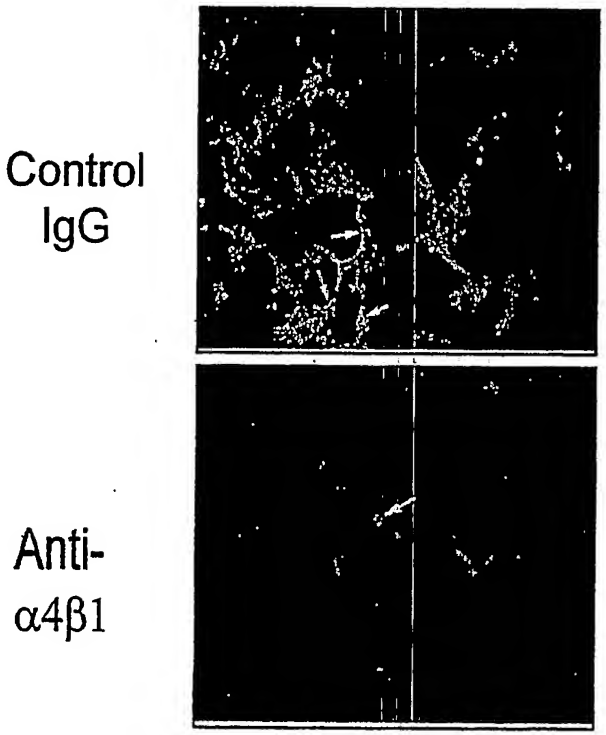
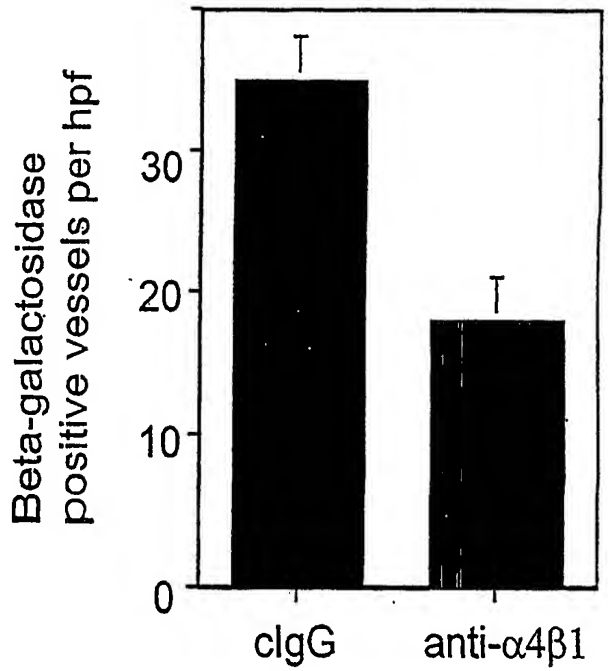
Fig. 31

Integrin α4β1 promotes EPC contributions to angiogenesis *in vivo*





Green = beta-galactosidase +
Red = CD31+

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Fig. 32

α4β1 promotes EPC extravasation and participation in vessel formation

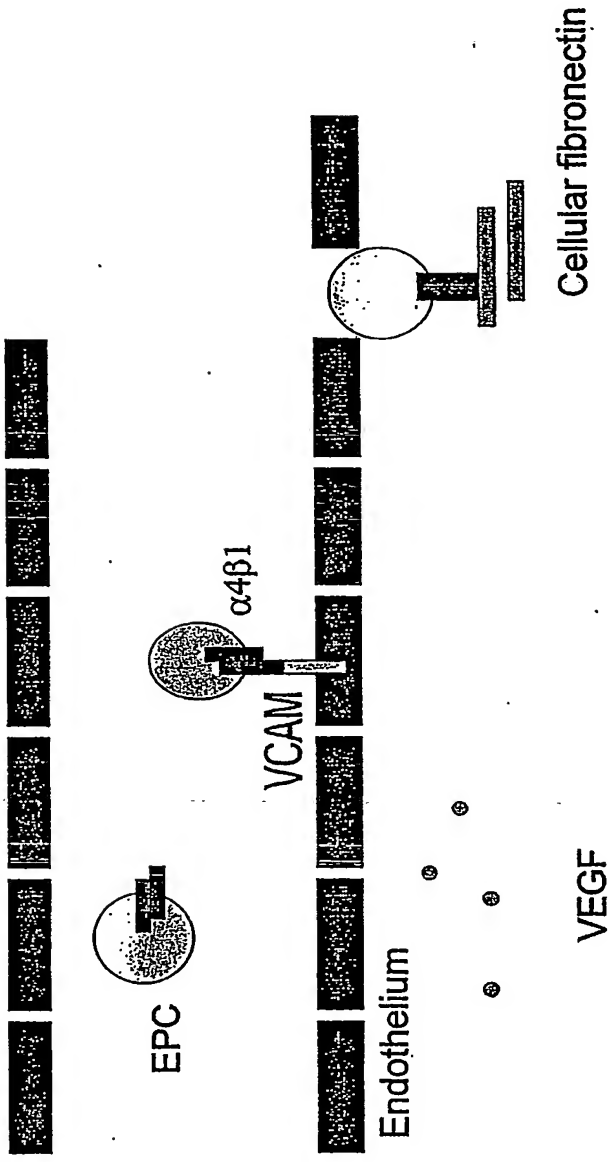

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Fig. 33

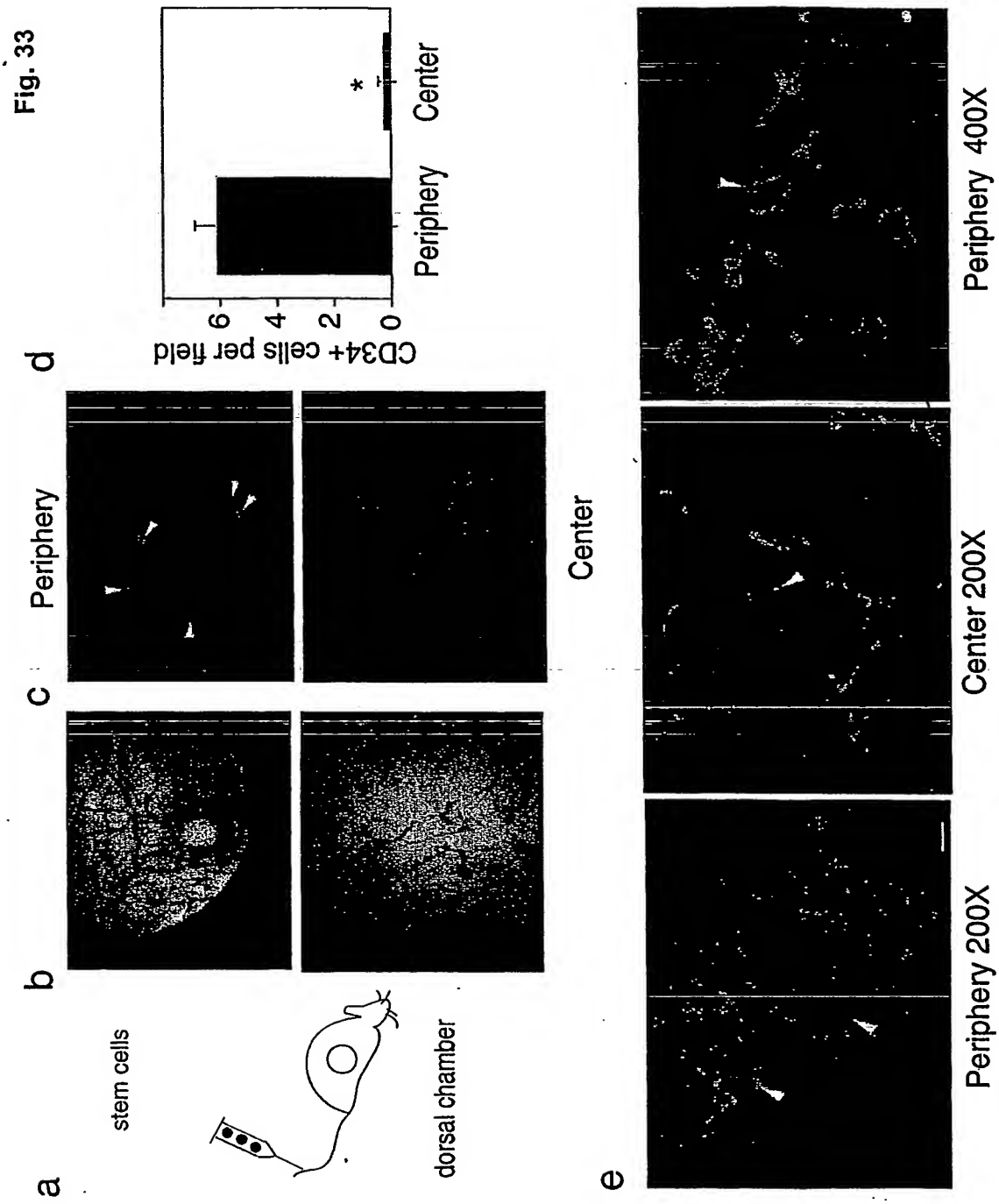
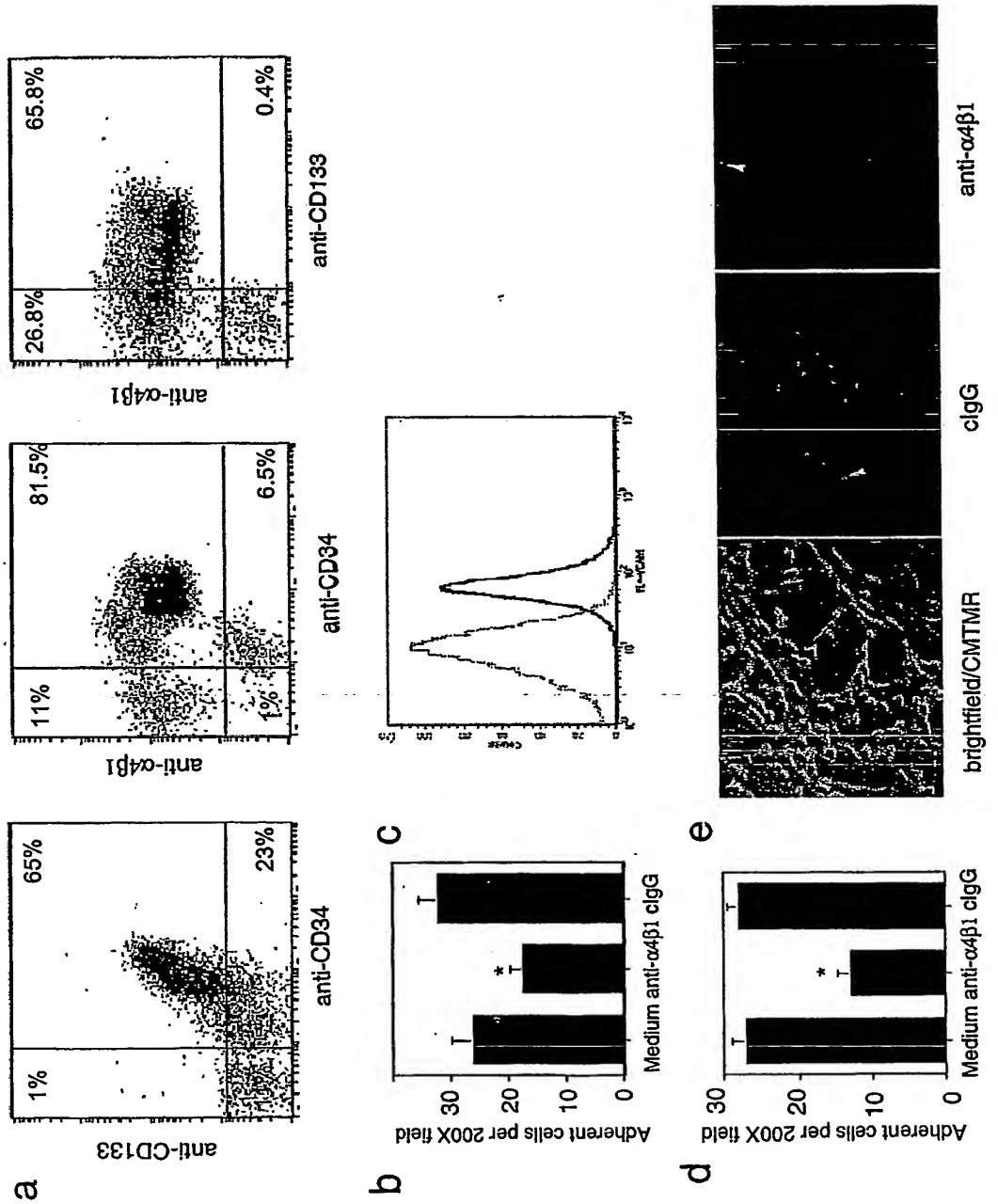


Fig. 34


a
anti-CD133
anti-CD34
anti-α4β1
1%
65%
23%
11%
81.5%
6.5%
26.8%
65.8%
0.4%
b
Adherent cells per 200X field
Medium anti-α4β1 cIgG
c
d
e
brightfield/CMTMR
cIgG
anti-α4β1

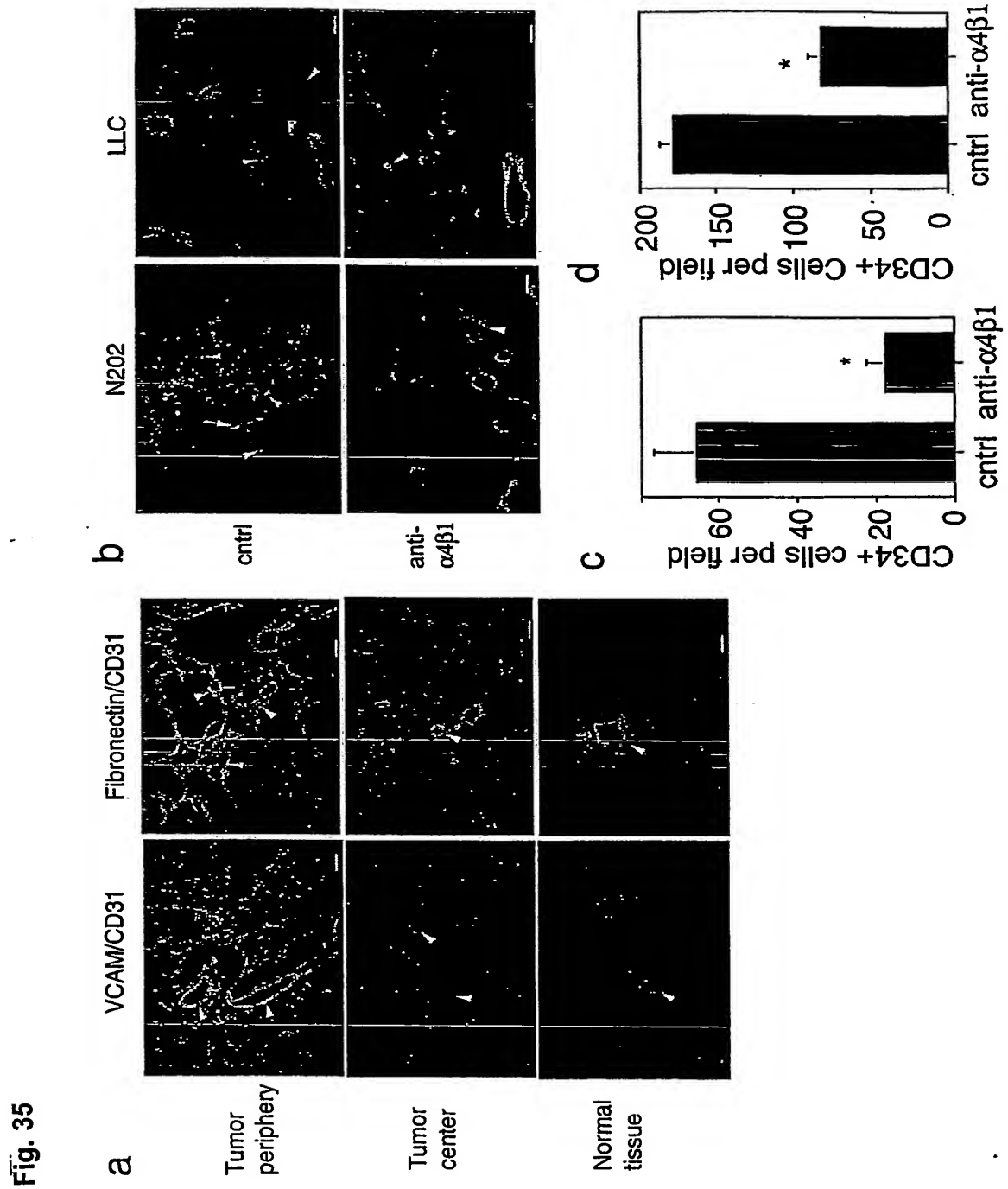

a
VCAM/CD31
Fibronectin/CD31
Tumor periphery
Tumor center
Normal tissue
b
N202
LLC
cntrl
anti-α4β1
c
CD34+ cells per field
0
20
40
60
cntrl
anti-α4β1
d
CD34+ Cells per field
0
50
100
150
200
cntrl
anti-α4β1

Fig. 35

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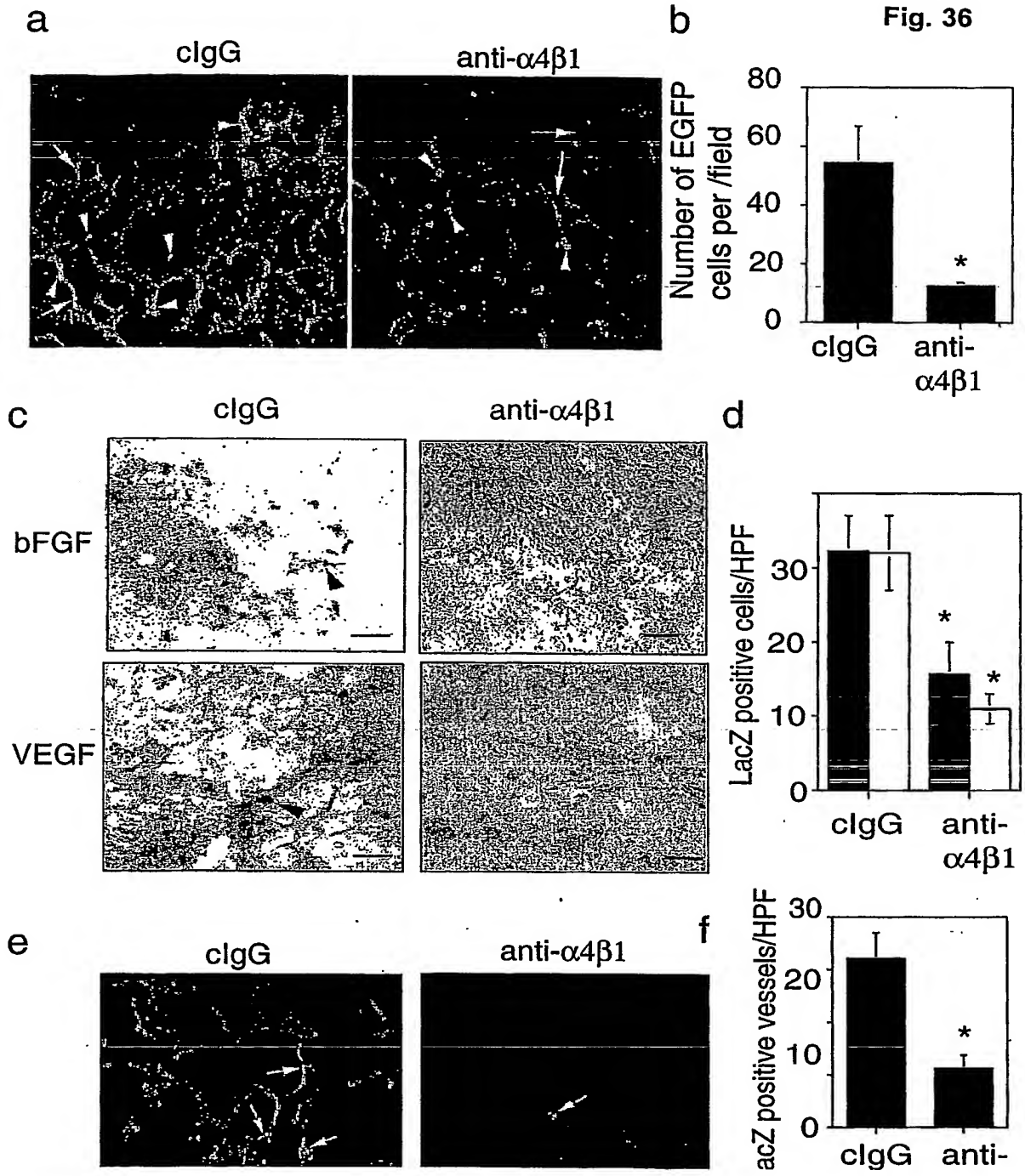
Fig. 36